2.2 STRESS

The term *stress* has become an often cited expression in describing the lifestyle of today's Western society. The concept of *stress* helps to explain the multiple bodily and psychological complaints of (yet) unknown origin (Pohlman & Becker, 2006). An acute, short-term response to stress is associated with positive influences on health and increases immunological function and thus ensures an organism's survival. The sustained (i.e. chronic) stress experience and its biological consequences are associated with negative influences on psychological and physiological health (e.g. Esch, Stefano, Fricchione, & Benson, 2002a; 2002b; 2002c; McEwen, 1998, 2008). Conservative estimates suggest that stress accounts for approximately 30% of the overall costs of illnesses and accidents across Western nations (Nater, Gaab, Rief, & Ehlert, 2006).

In the following, a brief introduction to the most prominent stress concepts will be outlined in order to provide a better understanding of how the term *stress* is used in health sciences. Furthermore, the physiological mechanisms that underlie the stress concept will be presented.

2.2.1 The concept of stress

The physiologist Walter Cannon is considered a pioneer in stress research. He coined the term of 'homeostasis', a concept that describes the sum of an individual's capacity to maintain most of the steady states in the organism by compensatory mechanisms to equilibrate environmental changes (Cannon, 1932). Stress, as an unspecific and uniform pattern of physiological processes, is considered to disturb the homeostatic equilibrium of the organism. If this is the case, the organism may react with 'fight-or-flight' responses (Cannon, 1915). Cannon suggested the sympathetic nervous system (SNS) to be the essential

homeostatic system. Some years later, Selye proposed a three-phasic process model, the ‘general adaptation syndrome’ (GAS), which describes stress in terms of external events that excite certain unspecific biological distress responses (Selye, 1950). He described this reaction by three consecutive steps: 1) alarm reaction (activation of SNS and the hypothalamus-pituitary-adrenal (HPA) axis), 2) resistance phase (organism is still in a state of heightened arousal, and adaptive mechanisms are intensified), and 3) exhaustion phase (gradual decrease of resistance to stress).

Both Cannon and Seyle proposed reaction-oriented stress theories, including non-specific and uniform stress reactions. These theories were of limited utility for the understanding of interindividual differences in biological stress responses. The increased awareness of individual differences to the same stressors initiated the development of extended theories. Mason, for instance, found that physical stressors influence the hormonal system only when the stressor is emotionally perceived as aversive (Mason, 1975; Mason, Giller, Koster, Ostroff, & Podd, 1986). Particular relevance in this context was given to the transactional stress model by Lazarus and colleagues (Lazarus & Folkman, 1984), in which psychological appraisal processes play a central role. The original concept has been modified over the past years. In the most recent version, the authors defined stress as 'a particular relationship between the person and the environment that is appraised by the person as taxing or exceeding his or her resources and endangering his or her well-being' (Lazarus & Folkman, 1984). Two central concepts, i.e. evaluation (primary appraisal) and coping (secondary appraisal), play an essential role. In the primary appraisal phase, an individual decides whether a situation is relevant or irrelevant, with the former being distinguished as benign or stressful. In the phase of the secondary appraisal, the individual considers alternative solutions, coping abilities, and consequences of a potential action. Additionally, coping strategies can be further divided into *problem-focused* or *emotion-oriented* coping strategies (Folkman, 1997). The former strategy is used when one is actively seeking to solve a problem; the latter is characterized by more passive and avoidant coping strategies.

Nevertheless, even when exposed to the same stressors, in terms of stress appraisal and coping, some individuals tend to respond more strongly to stressful situations than others. This disadvantageous pattern describes an individual's susceptibility to respond to a stressor with an immediate, intense, and long-lasting stress response (Schulz, Jansen, & Schlotz, 2005). In summary, (real or anticipated) stress emerges when perceived demands of a situation (primary appraisal) exceed the perceived resources (secondary appraisal) (Lazarus & Launier, 1981). Consequently, stress is the result of a cognitive appraisal process which, in a given situation, results in an emotional, physiological, and behavioral stress response.

McEwen finally introduced the term 'allostasis' and 'allostatic load' (McEwen, 1998). Allostasis, similarly to homeostasis, describes a process that actively maintains internal stability, but encompasses a wider concept and involves whole-organism mechanisms to preserve survival of the organism. Acutely, allostasis supports the adaptation to and the coping with a stressor – short-term stress is generally not harmful. Persisting allostasis, which is the maintaining of allostatic processes over too long periods, results in an 'allostatic load', i.e. maladaptive consequences of a sustained activation of primary regulatory systems (McEwen, 1998, 2000a). This framework also accounts for psychological factors, suggesting that cognitive processes moderate the physiological stress response and explain the existence of interindividual differences (McEwen, 2007, 2008).

2.2.2 Physiology of the stress systems

The entire stress system is understood as a complex physiological system that is located in the central nervous system (CNS) and peripheral parts of the organism. In the following, the major physiologic stress response systems in the body, the hypothalamus-pituitary-adrenal (HPA) axis and the autonomous nervous system (ANS), and their biomarkers, i.e. cortisol and salivary alpha-amylase (sAA), are described in detail.

2.2.2.1 The hypothalamus-pituitary-adrenal (HPA) axis

In order to provide a better understanding of the neuroendocrinological mechanisms of the stress response, the following paragraph will outline basic information about the HPA axis and its main biomarker, cortisol.

2.2.2.1.1 Anatomy and physiology of the HPA axis

The HPA is a regulatory system of the organism that links the CNS via the endocrine signaling with the periphery, mainly through the following three key hormones: the corticotropin-releasing hormone (CRH), adrenocorticotropin hormone (ACTH), and cortisol (Tsigos & Chrousos, 2002). These hormones are thought to ensure the maintenance of homeostasis. This is achieved through the activation and coordination of various psychological (e.g. memory, consolidation) and physiological (immune functioning, cardiovascular activation, glucose metabolism) processes, and emotional processing (Sapolsky, Romero, & Munck, 2000; Schulkin, McEwen, & Gold, 1994).